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## **CASE REPORT**

### **Guttural pouch leiomyosarcoma causing nasopharyngeal compression in a pony.**

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**Keywords:** horse; guttural pouch; nasopharyngeal compression; computed tomography; leiomyosarcoma.

## **Summary**

A 14-year old Connemara cross gelding presented with abnormal respiratory noise and exercise intolerance. Upper airway endoscopy, ultrasonography, radiography and computed tomography revealed a large mass within the left guttural pouch causing marked left dorsal nasopharyngeal collapse and displacement and compression of the right guttural pouch. The horse was euthanased and a post-mortem examination confirmed the above findings. Histological and immunohistochemical examinations of the mass confirmed a diagnosis of guttural pouch leiomyosarcoma, a lesion previously unreported at this site.

## **Introduction**

Abnormal respiratory noise and exercise intolerance is a relatively common clinical presentation in the horse and can be associated with structural, functional, inflammatory, infectious and neoplastic disorders of the nasal passages, sinuses, hard and soft palate, larynx and nasopharynx. The close anatomical proximity between the ventral floor of the guttural pouches and the dorsal nasopharyngeal roof means that guttural pouch distension can cause dorsal nasopharyngeal compression and is a differential diagnosis in such cases. Neoplasia of the guttural pouch is rare (Hance and Bertone 1993; Baptiste et al. 1996; Caswell and Williams 2007; Freeman 2015). This report describes the clinical, ancillary diagnostic and pathological findings in a case of primary guttural pouch leiomyosarcoma, a lesion that does not appear to have been previously described in horses.

## **Case history and clinical findings**

A 14-year old Connemara cross gelding, used for pleasure and low level competition, was presented for abnormal, harsh respiratory noise during ridden work and exercise intolerance which had become progressively worse over the preceding 2 weeks. It was reported that the horse had demonstrated episodes of coughing 4 months previously, which had improved with medical management and had been attributed to lower airway disease. On presentation, the gelding was bright and alert, with mild swelling of the parotid region bilaterally and a mild bilateral (but predominantly left sided) seromucoid nasal discharge. The submandibular lymph nodes were not enlarged. No abnormal respiratory noise was audible at rest, but inspiratory stridor was appreciated during light in-hand exercise.

## Investigation

Because of the above presenting signs, the horse was isolated pending further investigation of potential infectious causes, particularly *Streptococcus equi* subsp. *equi* infection. Upper airway endoscopy revealed marked dorsal nasopharyngeal collapse, greater on the left side, with marked reduction in the diameter of the nasopharynx rostral to, and overlying, the rima glottidis. Muroid discharge was seen to emanate from the left guttural pouch ostium, accumulating on the floor of the nasopharynx. Endoscopy of the right guttural pouch revealed marked compression of its medial compartment. A guttural pouch lavage was negative for *Streptococcus equi* subsp. *equi* on both culture and qPCR. Endoscopic access to the left guttural pouch was difficult as the ostium was collapsed and displaced medioventrally. Once access was gained, it showed loss of the normal air filled guttural pouch lumen that was replaced by a wall of soft tissue which prevented further endoscopic evaluation.

## Diagnostic Imaging

A latero-lateral radiograph of the pharyngeal region (Fig. 1A) identified a large, well defined, soft tissue opacity within the region of the guttural pouches, which extended caudally to the mid-point of C2 and ventrally to a level 1cm dorsal to the soft palate that was causing marked dorsal nasopharyngeal compression. There was a narrow margin of gas dorsal to the mass, believed to be air within the guttural pouches. Transcutaneous ultrasonography of the left parotid region caudal to the left temporomandibular joint revealed an ovoid, soft tissue mass approximately 3cm below the skin surface (Fig. 1B). This mass was of soft tissue echogenicity, well encapsulated and contained multiple, small, ovoid, hypoechoic regions resulting in a heterogeneous honey-comb appearance.

### **Surgical Biopsy**

The horse was sedated (detomidine [Medesedan<sup>®</sup>]<sup>a</sup> 0.01 mg/kg IV and butorphanol [Butador<sup>®</sup>]<sup>b</sup> 0.02 mg/kg IV) and local anaesthesia administered (lignocaine hydrochloride 2% and epinephrine acid tartrate 0.00198% [Lignol<sup>®</sup>]<sup>c</sup> 30ml). A modified Whitehouse approach was made to gain access to the left guttural pouch. Following incision into the pouch the base of a rounded, firm, soft tissue mass in the lateral compartment was palpable. An excisional biopsy was taken from the directly visualised ventral aspect of this mass and histopathology of cryostat and formalin fixed sections revealed fibrinous and neutrophilic inflammation with granulation tissue, fibrinoid vasculitis and thrombosis. However, it was deemed possible that these reactive and inflammatory microscopic changes may have been present towards the periphery of the mass and may not have been representative of the mass as a whole.

### **Advanced Diagnostic Imaging**

Computed Tomographic (CT) examination of the head (Fig. 2A-D) was performed under standing sedation (as detailed above) including contrast CT using iopamidol [Niopam®]<sup>d</sup> 0.2 ml/kg, administered via a jugular catheter. A large, left lateralised, multi-lobular soft tissue mass with multiple, small, well-defined, ovoid, central, hypoattenuating regions and variable contrast enhancement was seen within the region of the left guttural pouch. The mass compressed the left guttural pouch and the medial aspect of the right guttural pouch and caused marked ventral displacement of the nasopharyngeal roof, resulting in significant narrowing of the nasopharynx consistent with that seen endoscopically. The left stylohyoid bone which was enveloped by the mass was mildly thickened and had well defined, smoothly irregular, periosteal new bone formation along its length. The administration of contrast medium clearly demonstrated the borders of the mass, which was surrounded by non-contrast enhancing, soft tissue attenuating material. The biopsy site was identified caudal to the mass lesion, and gas was seen tracking from the incision into the peripheral soft tissue attenuating material, however it did not breach the border of the mass. Following visualisation of the full extent of the mass on contrast CT no repeat attempts at surgical biopsy were made. Differential diagnoses based on the imaging findings included soft tissue neoplasia, such as haemangiosarcoma, squamous cell carcinoma or other neoplastic lesion and granuloma formation originating from pharyngeal or lymphoid tissue. Abscessation of the left retropharyngeal lymph nodes was considered unlikely due to the pattern of contrast enhancement.

## Outcome

Owing to the extensive nature of the mass and the difficulty of surgical access, combined with worsening stertor, the owner elected for euthanasia and the horse was submitted for post-mortem examination.

### **Post-mortem gross and histological examinations**

Grossly, a 14cm x 13.5cm x 9.5cm, bi-lobed, heterogeneous mass (Fig. 3) was present on the caudal wall of the left guttural pouch. The lateral portion of the mass that surrounded the left stylohyoid bone was mottled pink to yellow in colour, firm and fibrous. In contrast, the medial portion was variegated dark red to yellow in colour and contained multiple, variably sized cysts. Histology of the mass (Fig. 4) revealed an encapsulated, well demarcated, multi-lobulated, densely cellular, proliferation of cells. This was composed of broad interlacing fascicles of medium sized, spindle shaped cells within a very fine vascular stroma. The cells had indistinct cytoplasmic borders, moderate amounts of vacuolated or fibrillar eosinophilic cytoplasm, and a blunt ended oval nucleus with finely granular chromatin and a single eosinophilic nucleolus. They exhibited strongly positive immunohistochemical labelling for vimentin, desmin and alpha-smooth muscle actin with negative labelling for cytokeratin (Fig. 5A-D). There was mild anisocytosis and anisokaryosis, with very rare karyomegaly, multinucleated cells, and less than 1 mitotic figure in ten high power fields (x400). Within the mass there were also large areas of coagulative necrosis and haemorrhage. **Local capsular invasion by neoplastic cells was visible following alpha-smooth muscle actin immunohistochemistry. There was no visible evidence of vascular or lymphatic invasion.**

### **Diagnosis**

These histological and immunohistochemical features enabled a definitive diagnosis of guttural pouch leiomyosarcoma to be made.

## Discussion

This report represents an addition to our limited existing knowledge of guttural pouch neoplasia in the horse, and also highlights the important contribution of advanced imaging modalities to the investigation of such cases. Computed tomography (CT) is an established modality for diagnosing diseases of the equine head and standing CT examination is becoming **more widely** available. In particular, CT is increasingly used in the assessment of dental disorders, head tumours and sino-nasal problems (Perrier et al. 2010; Puchalski 2012). The use of intravenous contrast material in the standing horse has previously been described (Dakin et al. 2014), however this appears to be the first report indicating its usefulness in a clinical case. Contrast administration allowed visualisation of the cystic nature of the mass and differentiation of the true margins of the mass from the surrounding soft tissues. **The ability to visualise the true margins of the mass and the biopsy site provided an explanation for the non-representative biopsy. Although there was a mild imaging artefact from the surgical site this did not impact significantly on the diagnostic usefulness of this technique. Surgical artefact can of course be avoided by undertaking advanced diagnostic imaging prior to biopsy, however, in this case the impetus to progress to more advanced imaging was in part, prompted by the non-representative biopsy result. Although ultrasound and/or endoscopy are also useful adjuncts to the attainment of targeted surgical biopsies, their usefulness was precluded in this case by limited access restricting the tissue available for biopsy to the periphery of the ventral aspect of the mass which could already be directly visualised.** The CT appearances of an invasive temporomandibular joint, guttural pouch and



calvarial tumour (Perrier et al. 2010), and sinonasal tumours (Cissell et al. 2012) have been described previously, however this appears to be the first report of a primary guttural pouch neoplasm identified using ante-mortem standard and contrast CT. In this case, **contrast** CT provided superior definition of the margins of the mass when compared to endoscopy, radiography and ultrasonography that was integral in the decision to euthanase the horse due to the extent of the mass and its surgically inaccessible location.

Equine tumours are uncommon, with an overall incidence of 2-3% in the general population (Hance and Bertone 1993). Neoplasia of the guttural pouch is particularly rare, and in the few reported cases, affected horses tended to be older than 10 years (Baptiste et al. 1996; Scarratt and Crisman 1998). Possibly due to their rarity, no breed or sex predilection has been identified. Tumours reported include; haemangioma (Greene and O'Connor 1986), haemangiosarcoma (Baptiste et al. 1996), melanoma (Hance and Bertone 1993; Baptiste et al. 1996; Fintl and Dixon 2001; Metcalfe et al. 2013), fibroma (Merriam 1972) and squamous cell carcinoma (Trigo and Nickels 1981; Perrier et al. 2010). The majority of these reports described malignant neoplasms, which were often a result of metastasis, especially those involving melanoma (Baptiste et al. 1996; Scarratt and Crisman 1998; Metcalfe et al 2013). The presence of invasive metastatic disease, restricted surgical access, multiple adjacent major neurovascular structures and limited medical options warrants a grave prognosis and most horses are eventually euthanased (Hance and Bertone 1993) **as occurred here. Given the rarity of these tumours, the usefulness of alternative treatments such as radiotherapy is unknown. It may be speculated that they would be of most use early in the course of disease when tumours are small and invasion is minimal but complete excision is still prevented by limited surgical access and the multiple nerves and vasculature in this area. However, as in this particular case, significant clinical signs may not be detectable until late in the course of disease when the mass is already well developed.** There are several reports of

leiomyosarcoma in the horse within the digestive (Livesey et al. 1986; Clem et al. 1987; Mair et al. 1990; Boy et al. 1992; Laugier et al. 2004) and urogenital tracts (Lofstedt et al. 1987; Allison and Moeller 1999; Hurcombe et al. 2008), most likely because these organ systems contain a significant smooth muscle component. Other reported leiomyosarcoma locations include pulmonary (Rossdale et al. 2004; Davis and Rush 2013), sino-nasal (Veraa et al. 2009) and multicentric sites (MacGillivray et al. 2003). Leiomyosarcomas are frequently invasive and may undergo visceral metastasis (Cooper and Valentine 2002) warranting a poor prognosis, although no preferential sites of metastasis have been identified. Histologically, they may be well differentiated and relatively well demarcated, retaining many features of normal smooth muscle and resembling benign leiomyoma, or less so, with marked cellular pleomorphism, including multinucleate forms and smaller, less well organised, fascicles. As in this case, areas of tumour necrosis are common (in contrast to leiomyoma), resulting in a cystic appearance often accompanied by haemorrhage, oedema and inflammation (Cooper and Valentine 2002). Despite a relatively low mitotic index, the presence of marked tumour necrosis and multinucleate forms combined with the locally invasive behaviour (visible after immunohistochemical staining for alpha-smooth muscle actin) were deemed consistent with a well differentiated, malignant mesenchymal (likely smooth muscle) tumour. Suspected malignant smooth muscle neoplasia in previously unrecognised anatomical locations, and the presence of poorly differentiated forms, can make distinction from other mesenchymal tumours such as fibrosarcoma, malignant nerve sheath tumour, haemangiosarcoma, rhabdomyosarcoma and undifferentiated sarcoma challenging and definitive diagnosis requires immunohistochemical staining. Positive vimentin staining combined with negative staining for cytokeratin can confirm the presence of mesenchymal neoplasia, whilst excluding the presence of poorly differentiated epithelial tumours. Concurrent positive staining for desmin and alpha-smooth muscle actin is strongly suggestive of smooth muscle, and even

though striated muscle frequently expresses positive desmin staining, it is rarely positive for alpha-smooth muscle actin (Cooper and Valentine 2002).

## **Conclusions**

Despite their relative infrequency, neoplasms including leiomyosarcoma should be considered a differential diagnosis in cases of guttural pouch disease. The use of CT can play an important role in the assessment of guttural pouch masses where endoscopic access is limited.

## **Authors' declaration of interests**

No conflicts of interest have been declared.

## **Ethical animal research**

Informed consent was obtained from the owner by means of the standard consent form utilised in our hospital. The post-mortem examination and use of the resultant material was discussed with the owner.

## **Source of funding**

No funding was provided for this study

## **Authorship**

LM, RJMR, BCM and PMD contributed directly to case management; SJD and JDP provided pathological analysis and interpretation; drafting of the manuscript was undertaken by SJD and LM. All authors contributed to the critical revision of this article and have approved the final version.

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### **Manufacturers' addresses**

<sup>a</sup> Medesedan<sup>®</sup>, Virbac Ltd, Suffolk, UK.

<sup>b</sup> Butador<sup>®</sup>, Chanelle UK, Berkshire, UK.

<sup>c</sup> Lignol<sup>®</sup>, Dechra Veterinary Products Ltd, Shropshire, UK.

<sup>d</sup> Niopam<sup>®</sup>, Bracco UK, Buckinghamshire, UK.

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## Figure Legends

Fig. 1A) **Latero-lateral** radiograph of the caudal aspect of the head, showing a large, well defined, ovoid soft tissue mass within the region of the guttural pouches. There is a narrow gas lucency dorsal to the mass (white arrow), which is likely to be air within the guttural pouches. The ventral margin of the mass is causing marked compression of the nasopharynx (between black arrowheads). B) Ultrasonographic image obtained with the probe oriented vertically over the left parotid region caudal to the mandibular ramus. The mass is of soft tissue echogenicity, containing multiple, small, ovoid, hypoechoic regions (white arrows).

Fig. 2 Transverse computed tomographic images (A & B), sagittal (C) and dorsal (D) 3D reconstructions. All images are viewed in a soft tissue window, with left to the right of images A, B & D.

A) Transverse pre-contrast image showing a large heterogeneously soft tissue opacity attenuating mass (dorsal and axial margins denoted by white arrows) occupying the majority of the left guttural pouch and causing the marked compression of the right guttural pouch, with marked right deviation of the midline septum to the level of the right stylohyoid bone. There is marked compression of the nasopharynx (x). B) Transverse post-contrast image at a similar level; exact slice matching is not possible as the horse was repositioned during contrast injection. The mass shows moderate peripheral contrast enhancement (white arrows). The centre of the mass demonstrates patchy, mild contrast enhancement, with some non-contrast enhancing regions. Marked nasopharyngeal compression is again seen (x). The non-contrast enhancing regions peripheral to the mass were interpreted as reactive tissue or oedema secondary to the mass. C) Sagittal post-contrast reconstruction obtained just to the left of midline, demonstrating the rostro-caudal extent of the mass (between white arrows). Peripheral contrast enhancement is again seen with patchy contrast enhancement within the mass. D) Dorsal pre-contrast reconstruction obtained at the dorsoventral midpoint of the mass, showing marked right deviation of the midline guttural pouch septum and marked compression of the right guttural pouch.

Fig. 3 Guttural pouch mass, dorsal view, showing a smooth surfaced, bi-lobed appearance with firm fibrous lateral portion (lateral is to the right) and cystic medial portion.



Fig. 4 Histological section from the guttural pouch mass showing interlacing fascicles of neoplastic spindle shaped cells, HE x100, scale bar = 200 $\mu$ m.

Fig. 5 Histological section of the guttural pouch mass showing neoplastic spindle shaped cells exhibiting negative immunohistochemical staining for cytokeratin (A) and strongly positive staining for vimentin (B), desmin (C) and alpha-smooth muscle actin (D) x200, scale bar = 100 $\mu$ m.